BstNI. The digested products were run on a 4% agarose gel, stained with ethidium bromide, and visualized by UV transillumination. The expected digestion product sizes were 220 bp for Gly972 homozygotes, 164 bp and 56 bp for Arg972 homozygotes and 220 bp, 164 bp and 56 bp for heterozygotes.

REMARKS

In this Response, Claims 2 and 4 are pending. Claims 2 and 4 are rejected and Claims 1 and 3 have been withdrawn from consideration. In this Response, Claims 2 and 4 have been amended and Claims 1 and 3 have been cancelled without prejudice as non-elected. No new matter has been added to the application by these amendments.

Claims 1-4 have been subjected to a telephonic Restriction Requirement. Applicant herein confirms that Group II, Claims 2 and 4, have been elected for prosecution. Applicant herein cancels Claims 1 and 3 (Groups 1 and 3, respectively) as non-elected.

The Examiner has objected to the specification as containing sequences that are encompassed by the definitions of 37 C.F.R. 1.821(a)(1) and (a)(2). Applicant attaches to this Response both a paper and computer-readable copy of a sequence listing for these sequences. Additionally, Applicant has presented amendments to the specification in this Response. In light of the attached sequence listings and amendments, Applicant requests that the objections to the specification be withdrawn.

Claims 2 and 4 have been rejected under 35 U.S.C. 112, second paragraph, as indefinite. The Examiner has taken the position that these claims are indefinite because

they recite "having a "12" genotype" and "having a "11" genotype," respectively. The Examiner has advanced that the specification does not contain an adequate definition of these terms. It is submitted that this rejection is not well taken. It is further submitted that the terms "'11' genotype" and "'12' genotype" would be readily understood by one of ordinary skill in the art. Attached to this Response is GENBANK sequence identifying human myostatin mRNA. It is further submitted that it would be understood by one of ordinary skill that the "11" genotype would contain Lys at position 153 and that "12" would contain arginine based upon the teachings of page 7, line 11 of the present specification.

Additionally, it is submitted that the MPEP states in section 2164.05(a) that the "specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public." Therefore, it is submitted that because one of ordinary skill would already know what "11" and "12" genotypes were referring to, Applicant was not required to define these terms in the specification. Therefore, it is submitted that the rejection is not well taken and it is requested that the rejection be withdrawn.

It is also noted that Claims 2 and 4 have been rejected as indefinite because the term "a myostatin exon 2 gene" is unclear. It is submitted that this term is intended to refer to the second exon of the myostatin gene. Applicant has amended both Claims 2 and 4 to clarify the meaning of the claims. In light of the above explanation and the amendments to Claims 2 and 4, it is requested that the rejection of Claims 2 and 4 be withdrawn.

Claims 2 and 4 have been rejected under 35 U.S.C. 112, first paragraph, as not enabled by the specification. The Examiner has advanced that the specification fails to adequately define "11" and "12" genotypes and has taken the position that this supports the rejection of Claims 2 and 4 as not enabled. It is submitted that the statements made above regarding the knowledge in the art of these terms and what they encompass render this argument not well taken. Therefore, Applicant relies on the arguments presented above and requests that this basis for the rejection be withdrawn.

The Examiner has also supported the rejection on the basis that a relationship between particular alleles in the second exon of the myostatin gene and a particular phenotype (the ability to improve cholesterol levels with extensive exercise or the ability to improve diabetes status with extensive exercise) has not been established. The Examiner has also argued that while the prior art is silent as to the polymorphisms in the human myostatin gene, it has determined that the establishment of a relationship between a polymorphism and a phenotype is highly unpredictable. The Examiner has presented the Hacker and Pennisi references in support of her position.

The Examiner has advanced that Hacker was unable to confirm an association between a gene polymorphism and ulcerative colitis in a case where prior studies suggested a relationship would exist since the relationship had been identified in a different population. Additionally, the Examiner has advanced that Pennisi teaches that even where an association between a particular gene and a disease state is known to exist, it was difficult to associate SNP's with disease states or to even identify key genes as being associated with disease.

It is submitted that the cited references are not relevant to the present invention. It is noted that the Hacker reference is directed towards a method for determining a genetic predisposition for ulcerative colitis. This is irrelevant to the method of the present invention. In the presently claimed methods, the subjects are already known to possess the hypochlolesteremia or diabetes. Therefore, the presently claimed method is examining something completely different from that of the Hacker reference. The present method examines the genotype of an individual which possesses the disease for a "11" or "12" genotype (depending on the disease) for the second exon of the myostatin gene, which signifies that the individual would respond better to exercise than an individual that did not possess this genotype. Thus, Hacker and the present invention are directed towards entirely different concepts, the identification of a subject with a predisposition to a disease and the identification of a subject who will respond better to a treatment.

Additionally, it is noted that Hacker does not address myostatin exon genotypes at all. Therefore, it is submitted that Hacker does not present any information that would lead one of ordinary skill to believe that the present invention is not enabled. In other words, while Hacker may prove that there was not correlation between a certain genotype and the onset of ulcerative colitis, there is no evidence in Hacker that the present invention will not work. Therefore, in absence of any evidence in Hacker regarding the claimed invention, it is submitted that the rejection is not well taken and it is requested that it be withdrawn.

It is noted that Pennisi is also cited by the Examiner. As Pennisi is a secondary reference to Hacker (the primary reference), it is submitted that the above arguments overcoming Hacker are sufficient to overcome this secondary reference as well. Additionally, it is noted that the arguments presented above regarding Hacker are relevant to Pennisi. That is, Pennisi also does not present any information regarding the enablement of the claimed invention. Pennisi does not discuss genotypes of the second exon of the myostatin gene. Therefore, there is no evidence in Pennisi that the present invention would not work. For this reason, it is submitted that the present invention is enabled and it is requested that this rejection be withdrawn.

The Examiner has also objected to the statistical data presented in the specification. It is submitted that the presented data is sufficient for one of ordinary skill to determine the efficacy of the claimed methods. Additionally, one of ordinary skill would be able to extrapolate the information from data that would be presented in a statistical analysis of the same. Therefore, it is submitted that the present invention is enabled and that this basis of the rejection is improper.

Finally, the Examiner has objected to the term "extensive exercise" as any length of time is encompassed by the claim language, however, only nine months of exercise is shown in the data. The Examiner has alleged that shorter periods of exercise would be highly unpredictable in achieving improvement in diabetes or cholesterol status.

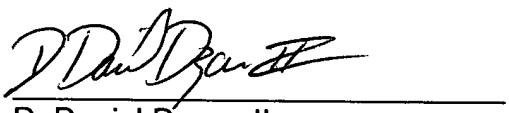
Applicant submits that this basis for the rejection is not well taken. The term "extensive exercise" is defined in the specification, and one of ordinary skill would have no problem understanding this term. Additionally, the Examiner has presented no

support for this rejection other than her opinion. This is improper. See *In re Marzocchi*, 169 USPQ 367 (CCPA 1971) (A specification disclosure must be taken as being in compliance with the enablement requirement unless there is a reason to doubt the objective truth of the statements contained therein). Therefore, it is submitted that there is no basis to support this rejection. It is requested that the rejection be withdrawn.

Should the Examiner deem that any further action by the Applicants would be desirable for placing this application in even better condition for issue, the Examiner is requested to telephone Applicants' undersigned representative at the number listed below.

In the event this paper is not timely filed, Applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300, referring to client-matter number 108172-00071.

Respectfully submitted,



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Fax: (202) 638-4810

Enclosures: Marked-Up Copy of the Claims
GENBANK Sequence
Petition for Extension of Time (2 months)
Computer-Readable Copy of the Sequence Listing
Paper Copy of the Sequence Listing

MARKED UP COPY OF CLAIMS

2. (Amended) A method of improving cholesterol levels in a subject in need of such improvement, the method comprising:

identifying a subject with hypercholesteremia or at risk of developing hypercholesteremia having a "12" genotype for [a] the second exon of the myostatin [exon 2] gene, wherein the subject is in need of improved cholesterol levels; and

engaging the subject in extensive exercise training for a period of time sufficient to improve the cholesterol levels in the subject.

4. (Amended) A method of improving diabetes status in a subject in need of such improvement, the method comprising:

identifying a subject with diabetes or at risk of developing diabetes having an "11" genotype for [a] the second exon of the myostatin [exon 2] gene, wherein the subject is in need of improved diabetes status; and

engaging the subject in extensive exercise training for a period of time sufficient to improve the diabetes status in the subject.

Entrez Nucleotide

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Boo

Search Nucleotide for Go Clear

Limits Preview/Index History Clipboard Details

Display default Show: 20 Send to File Get Subsequence

1: AF019627. Homo sapiens myos...[gi:2623581] Links

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  AUTHORS   McPherron,A.C. and Lee,S.J.
  TITLE     Double muscling in cattle due to mutations in the myostatin gene
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 94 (23), 12457-12461 (1997)
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  TITLE     Direct Submission
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